Media & Investor Release

Majority of newborn babies with spinal muscular atrophy (SMA) treated with Roche's Evrysdi able to sit independently after 1 year of treatment

- **RAINBOWFISH study met its primary endpoint with 80% of babies sitting without support for at least five seconds after 1 year of Evrysdi treatment – without treatment these babies would never be able to sit**
- **All babies were able to swallow and feed orally and none required permanent ventilation**
- **Evrysdi is the only non-invasive SMA therapy and is approved in over 100 countries with more than 11,000 patients treated globally**

Basel, 04 October 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today presented positive results from the primary analysis of the ongoing RAINBOWFISH study assessing the efficacy and safety of Evrysdi® (risdiplam) in babies with pre-symptomatic SMA (n=26), aged from birth to six weeks. The data were presented at the 28th World Muscle Society (WMS) Congress, 3-7 October 2023.

"Evrysdi is the only non-invasive SMA treatment and can be used within hours of birth, potentially allowing these babies to sit, stand and walk, similar to healthy individuals," said Levi Garraway, M.D., Ph. D., Roche's Chief Medical Officer and Head of Global Product Development. "Evrysdi has now demonstrated its safety and efficacy in babies, children and adults and these compelling data continue to reinforce our confidence in this treatment."

Clinical studies show that the loss of motor neurons may begin before symptoms start so initiating treatment early is critical for better outcomes. The RAINBOWFISH study included babies with two or more copies of the *SMN2* gene. Generally, the lower the number, the more severe the disease.

The study met its primary endpoint with 80% of the primary efficacy population (n=5) sitting without support for at least five seconds after 1 year of Evrysdi treatment, assessed by Bayley Scales of Infant and Toddler Development, third edition (BSID-III). The primary efficacy population included babies with two *SMN2* copies and a CMAP amplitude of ≥1.5 mV at baseline. CMAP amplitude measures the muscle response to a stimulus, and a low score correlates with symptom onset in SMA patients and worse functional outcomes. Of the 26 babies in the study, 81% could sit independently for 30 seconds, including all patients with low CMAP amplitude at baseline (<1.5 mV) and the majority were standing and walking. Without treatment, children with Type 1 SMA would never be expected to sit.

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RAINBOWFISH was the first trial to assess cognition with a standardised scale (BSID) as an exploratory endpoint and results showed cognitive skills typical of normal child development after 1 year of Evrysdi treatment, assessed by BSID-III.

Adverse events (AEs) were more reflective of the age of the babies than underlying SMA. The majority of AEs were not considered treatment-related, and there were no deaths or AEs leading to withdrawal or treatment discontinuation. The most common AEs were teething, COVID-19, pyrexia, gastroenteritis, eczema and constipation. The AEs observed in the RAINBOWFISH primary analysis are generally consistent with those AEs seen in other Evrysdi trials in SMA.

“These data reinforce the value of beginning treatment for SMA before symptoms appear, with the goal of preserving motor neurons while they are still abundant,” said Richard Finkel, M.D., RAINBOWFISH Principal Investigator and Director of the Experimental Neuroscience Program at St. Jude Children’s Research Hospital. “Coupled with widespread newborn screening programs, early treatment could counteract the effects of the disease to give babies with pre-symptomatic SMA the best possible start in life.”

Roche is also investigating Evrysdi in combination with an anti-myostatin molecule, which is designed to promote muscle growth, among SMA patients 2-10 years of age in the Phase 2/3 MANATEE trial.

About Evrysdi® (risdiplam)

Evrysdi is a survival motor neuron 2 (*SMN2*) splicing modifier designed to treat SMA caused by mutations in chromosome 5q that lead to survival motor neuron (SMN) protein deficiency. Evrysdi is administered daily at home in liquid form and non-invasively by mouth or by feeding tube.

Evrysdi is designed to treat SMA by increasing and sustaining the production of SMN protein in the central nervous system (CNS) and peripheral tissues. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons and core motor functions such as swallowing, speaking, and breathing.

Evrysdi was granted PRIME designation by the European Medicines Agency (EMA) in 2018 and Orphan Drug Designation by the U.S. Food and Drug Administration in 2017. In 2021, Evrysdi was awarded Drug Discovery of the Year by the British Pharmacological Society as well as the Society for Medicines Research Award for Drug Discovery. Evrysdi is currently approved in over 100 countries, and the dossier is under review in a further 15 countries.

Evrysdi is currently being evaluated in five multicentre trials in people with SMA:

- FIREFISH (NCT02913482) – an open-label, two-part pivotal clinical trial in infants with Type 1 SMA. The study met its primary endpoint.
- SUNFISH (NCT02908685) – a two-part, double-blind, placebo-controlled pivotal study in people aged 2-25 years with Types 2 or 3 SMA. The study met its primary endpoint.
- JEWELFISH (NCT03032172) – an open-label exploratory trial designed to assess the safety, tolerability, pharmacokinetics and pharmacodynamics in people with SMA aged 6 months to 60 years who received other investigational or approved SMA therapies for at least 90 days prior to receiving Evrysdi. The study has completed recruitment (n=174).
- RAINBOWFISH (NCT03779334) – an open-label, single-arm, multicentre study, investigating the efficacy, safety, pharmacokinetics, and pharmacodynamics of Evrysdi in babies (n=26), from birth to six weeks of age (at first dose) with genetically diagnosed SMA who are not yet presenting with symptoms. The study is fully enrolled.
- MANATEE (NCT05115110) – a global phase 2/3 clinical study to evaluate the safety and efficacy of GYM329 (RG6237), an anti-myostatin molecule targeting muscle growth, in combination with Evrysdi for the treatment of SMA in patients 2-10 years of age. The FDA Office of Orphan Products Development granted GYM329 Orphan Drug Designation for the treatment of patients with SMA in December 2021. The study is currently recruiting.

In addition to bringing Evrysdi to people around the world, Roche also leads its clinical development as part of a collaboration with the SMA Foundation and PTC Therapeutics.

About SMA

SMA is a severe, progressive neuromuscular disease that can be fatal. It affects approximately one in 10,000 babies and is the leading genetic cause of infant mortality. SMA is caused by a mutation of the survival motor neuron 1 (*SMN1*) gene, which leads to a deficiency of SMN protein. This protein is found throughout the body and is essential to the function of nerves that control muscles and movement. Without it, nerve cells cannot function correctly, leading to muscle weakness over time. Depending on the type of SMA, an individual's physical strength and their ability to walk, eat or breathe can be significantly diminished or lost.

About Roche in Neuroscience

Neuroscience is a major focus of research and development at Roche. Our goal is to pursue groundbreaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases.

Roche is investigating more than a dozen medicines for neurological disorders, including multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease and Duchenne muscular

dystrophy. Together with our partners, we are committed to pushing the boundaries of scientific understanding to solve some of the most difficult challenges in neuroscience today.

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognising our endeavour to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

For more information, please visit www.roche.com.

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